Amendments to the Specification:

Please replace the paragraph beginning at page 5, line 2, with the following:

Figure 1 is a schematic of PAG and certain mutants described herein. The cytoplasmic domain of PAG contains several sites for tyrosine phosphorylation, one of which binds the inhibitory kinase, csk. The amino acids comprising the C-terminal PDZ-ligand (PL) of PAG are shown (-ITRL; SEQ ID NO:1), in addition to those of the mutants constructed: PAG C-ARA (-IARA; SEQ ID NO:2) and PAG ΔPL(-I). A FLAG epitope was introduced downstream of the CD8 leader sequence to facilitate expression analysis.

Please replace the paragraph beginning at page 10, line 32, with the following:

As used herein, the term "PDZ domain" refers to protein sequence (i.e., modular protein domain) of approximately 90 amino acids, characterized by homology to the brain synaptic protein PSD-95, the Drosophila septate junction protein Discs-Large (DLG), and the epithelial tight junction protein ZO1 (ZO1). PDZ domains are also known as Discs-Large homology repeats ("DHRs") and GLGF (SEQ ID NO:5) repeats). PDZ domains generally appear to maintain a core consensus sequence (Doyle, D. A., 1996, Cell 85: 1067-1076).

Please replace the paragraph beginning at page 21, line 11, with the following:

To test directly the role of the PDZ-binding motif present in PAG (ITRL; SEQ ID NO:1), two C-terminal mutants expected to abolish PDZ binding were prepared (FIG. 1). One mutant, termed PAG C-ARA, changes the critical threonine and leucine residues whose side chains extend into the PDZ binding pocket to alanine; the second, PAG ΔPL deletes the 3 most C-terminal residues, effectively removing the PDZ ligand motif from PAG. As described in Example 1, these two mutations in the binding motif resulted in an enhanced level of inhibition;

this result indicates that the PDZ interaction is important for relieving suppression by PAG on the TCR to allow for optimal activation. Thus, inhibiting the interaction between PAG and its PDZ-binding partner should decrease the sensitivity of the TCR and have a net suppressive effect on the T cell response (see FIGS. 2A and 2B).

Please replace the paragraph beginning at page 40, line 7, with the following:

To test the role of the PDZ-binding motif present in PAG (ITRL; SEQ ID NO:1) in T cell activation, we made two C-terminal mutants. In the mutant termed PAG C-ARA, we changed threonine and leucine to alanine; in PAG ΔPL the 3 most C-terminal residues were deleted, removing the PDZ ligand motif from PAG (FIG. 1). Plasmids encoding PAG, PAG C-ARA, and PAG ΔPL fusion proteins were transiently transfected into the Jurkat T cell leukemic line to assess their function, since T cell receptor signaling is dependent on the activity of the src kinases lck and fyn. In order to analyze TCR function, a Jurkat clone that contains a β-galactosidase reporter gene under the control of a triplicated form of the NFAT (nuclear factor of activated T cells) binding site was utilized. The activity of the NFAT transcription factor is as a good indicator of T cell activation since its activity depends on activation of both critical arms of the T-Cell Receptor (TCR) signaling cascade: calcium mobilization and activation of the ras pathway (27). As a control in the experiment we utilized a member of the tumor necrosis factor family of receptors, DR6, whose cytoplasmic domain has been removed to prevent it from influencing TCR activity in any way. Twenty-four hours after transfection, cells were stimulated with anti-TCR antibodies (FIG. 2A) or Ionomycin + PMA (FIG. 2B) for 6 hours, then analyzed for β-galactosidase activity and expression of the N-terminal FLAG epitope by flow cytometry. Results are expressed as the percentage of activated cells within the three designated populations: (a) Flag (-) or untransfected cells, and those that (b) expressed either low-intermediate, or (c) high levels of the transfected proteins, Flag (+).

Please replace the paragraph beginning at page 41, line 3, with the following:

Human shank 3 was cloned in the following manner. An expressed sequence tag (EST) was identified by a BLAST search of the human ESTs in Genebank using rat Shank 3 sequence (gi:11067398). Oligonucleotides based on the EST sequence (736 SHF – TGGATCCTTGAGGAGAAGACGGTG (SEQ ID NO:3); 737 shr - TGCAATTGTCGTCGGGGTCCAGATTC (SEQ ID NO:4)) were designed and the PDZ of human Shank was amplified by standard methods using PCR from Jurkat E6 T cell line cDNA. Amplified fragments were digested with BamHI and MfeI and cloned into the BamHI and EcoRI sites of pGEX-3X for expression (Amersham-Pharmacia).

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1-2, at the end of the application.